PATENT COOPERATION TREATY

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

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PCT

NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL PRELIMINARY EXAMINATION REPORT
(PCT Rule 71.1)

Date of mailing *(day/month/year)* 17.07.00	
Applicant's or agent's file reference 1038-938 MIS	**IMPORTANT NOTIFICATION**

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/CA99/00307	12/04/1999	14/04/1998

Applicant
CONNAUGHT LABORATORIES LIMITED et al.

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.

2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.

3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

4. **REMINDER**

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

Name and mailing address of the IPEA/	Authorized officer
European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Faux, K Tel.+49 89 2399-8062

Form PCT/IPEA/416 (July 1992)

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PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
1038-938 MIS		
International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/CA99/00307	12/04/1999	14/04/1998
International Patent Classification (IPC) or national classification and IPC C07K14/79		
Applicant CONNAUGHT LABORATORIES LIMITED et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 7 sheets, including this cover sheet.

   ☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 3 sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the report
   - II ☐ Priority
   - III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☒ Lack of unity of invention
   - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations suporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
11/11/1999	17.07.00
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Kalsner, I Telephone No. +49 89 2399 8708

Form PCT/IPEA/409 (cover sheet) (January 1994)

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/CA99/00307

I. Basis of the report

1. This report has been drawn on the basis of (*substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments.*):

Description, pages:

1-36 as originally filed

Claims, No.:

1-14 as received on 02/06/2000 with letter of 29/05/2000

Drawings, sheets:

1/73-73/73 as originally filed

2. The amendments have resulted in the cancellation of:

☐ the description, pages:
☐ the claims, Nos.:
☐ the drawings, sheets:

3. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

4. Additional observations, if necessary:

IV. Lack of unity of invention

1. In response to the invitation to restrict or pay additional fees the applicant has:

☐ restricted the claims.

☐ paid additional fees.

☐ paid additional fees under protest.

☐ neither restricted nor paid additional fees.

2. ☒ This Authority found that the requirement of unity of invention is not complied and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is

   ☐ complied with.

   ☒ not complied with for the following reasons:

   see separate sheet

4. Consequently, the following parts of the international application were the subject of international preliminary examination in establishing this report:

   ☒ all parts.

   ☐ the parts relating to claims Nos. .

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-14
	No:	Claims	
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-14
Industrial applicability (IA)	Yes:	Claims	1-14
	No:	Claims	

2. Citations and explanations

   see separate sheet

Ad Section IV: Lack of unity of invention

An international application must relate to one invention only or to a group of inventions so linked as to form a single general inventive concept.

Unity of invention is fulfilled only when there is a technical relationship among the inventions involving one or more of the same special technical features, special technical features being such features that define a contribution over which each of the claimed inventions, considered as a whole, makes over the prior art.

The following independent inventions have been identified:

Invention 1: Claims 1-15 insofar as they refer to a purified nucleic acid molecule encoding Tbp2 protein of strain *Moraxella catarrhalis* M35.

Invention 2: Claims 1-15 insofar as they refer to a purified nucleic acid molecule encoding Tbp2 protein of strain *Moraxella catarrhalis* 3.

Invention 3: Claims 1-15 insofar as they refer to a purified nucleic acid molecule encoding Tbp2 protein of strain *Moraxella catarrhalis* LES1.

The technical relationship between the three groups of invention can be seen in the fact that they all concern transferrin receptors.

As transferrin receptors are known in the art (D1) this relationship cannot be accepted to constitute a special technical feature as defined above.

Thus, the presently claimed subject-matter falls apart into the three groups of inventions identified above.

As the examination of the present application could be carried out without undue effort, the IPEA chose, according to Rule 68.1 PCT, not to invite the applicant to restrict or pay additional examination fees.

Ad Section V: Reasoned statement with regard to novelty, inventive step or

industrial applicability

1) **Amendments**

The amendments filed with the letter of 29 May 2000 are allowable under Art. 34(2)(b) PCT.

2) **Documents**

D1...WO-A-97 32980

3) **Novelty**

Claim 1 is directed to purified and isolated nucleic acid molecules encoding transferrin binding protein 2 (Tbp2) of various strains of *Moraxella catarrhalis* and defined by their DNA sequences as set out in SEQ ID NO: 1, 2 and 5.

As the specific sequences are not disclosed as such in the available prior art **claim 1** and any of the claims directly or indirectly dependent thereon (**claims 2-14**) are considered to meet the requirements of Art. 33(2) PCT.

4) **Inventive step**

Claims 1-14, however do not meet the requirements of Art. 33(3) PCT for the following reasons:

D1 discloses purified and isolated nucleic acid molecules encoding transferrin binding proteins (Tbp1 and Tbp2) of various *Moraxella catarrhalis* strains. These nucleic acid sequences are used to produce recombinant Tbp1 and Tbp2 for use in diagnostics and medical treatment.

The present application differs from D1 in the different strains of *Moraxella catarrhalis* as a source of the nucleic acid encoding Tbp2.

The problem to be solved by the present application can thus be seen in the

provision of transferrin binding proteins from other *Moraxella catarrhalis* strains.

D1 explicitly states that with the information given therein transferrin receptor genes can be identified from any species of *Moraxella* (p. 26, lines 22-26).

It thus is considered obvious for the skilled person having the information of D1 to clone further Tb proteins from *Moraxella* using the hybridisation conditions suggested in D1 (p. 26-28).

Claims 1-7 directed to isolated nucleic acid molecules encoding Tbp2 of *Moraxella*, vectors comprising such nucleic acid molecule, transformed host cells containing said vector, a method of forming recombinant Tbp2, a recombinant Tbp2 and an immunogenic composition comprising Tbp2 or Tbp2 encoding nucleic acid molecule are therefore not considered to involve an inventive step.

Furthermore, **claims 8 and 9**, which relate to methods for generating an immune response in a host and for determining the presence, in a sample, of nucleic acid encoding a Tbp of a strain of Moraxella, respectively, and **claim 10**, which relates to a diagnostic kit for determining the presence, in a sample, of nucleic acid encoding Tbp of a strain of *Moraxella* do not meet the requirements of Art. 33(3) PCT for the following reasons:

The use of a nucleic acid molecule, which is not inventive, in methods or diagnostic kits which are well known in the state of the art (D1) is not considered to invlove an inventive step.

Claims 11 and 12, which relate to the nucleic acid molecule of claim 1 and the recombinant Tbp of claim 6 for use as a medicine, and claims **13 and 14**, which relate to the use of a nucleic acid molecule of claim 1 and a recombinant transferrin receptor of claim 6 in the manufacture of a medicament for protection against an infection by a strain of *Moraxella*, do not meet the requirements of Art. 33(3) PCT for the following reasons:

D1 already discloses the use of Tbp2 for use as an active ingredient in a vaccine against infection with *Moraxella*, or the use of Tbp for the preparation of a

pharmaceutical composition (p. 19, lines 13-31). Hence, the use of the presently claimed nucleic acid molecules and their corresponding proteins as a medicine or for the manufacture of a medicament is not considered to involve an inventive step.

4) Industrial applicability

Claim 8 is directed to a method of treatment of the human or animal body. In this respect the following should be noted:

For the assessment of these claims on the question whether they are industrially applicable, no unified criteria exist in the PCT. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

5) Priority

The validity of the priority date of the present application has not been checked. If, however, the claimed priority is not valid, the documents cited in the International Search Report as "P" (Myers et al. (1998) Infection and Immunity 66: 4183-4192) would be relevant for assessment of novelty and inventive step of the present set of claims.

CLAIMS

What we claim is:

1. A purified and isolated nucleic acid molecule encoding a Tbp2 protein of a strain of *Moraxella* which strain is selected from the group consisting of *Moraxella catarrhalis* M35, 3 and LES1, said nucleic acid molecule having a DNA sequence selected from the group consisting of:

(a) a DNA sequence as set out in Figure 2, 4 or 6 (SEQ ID NOS: 1, 3 or 5) or the complementary DNA sequence thereto; or

(b) a DNA sequence encoding an amino acid sequence as set out in Figure 2, 4 or 6 (SEQ ID NOS: 2, 4 or 6) or the complementary DNA sequence thereto.

2. A vector adapted for transformation of a host comprising the nucleic acid molecule of claim 1.

3. The vector of claim 2 further comprising expression means operatively coupled to the nucleic acid molecule for expression by the host of said Tbp2 protein of a *Moraxella catarrhalis* strain M35, 3 or LES1.

4. A transformed host containing an expression vector as claimed in claim 3.

5. A method of forming a substantially pure recombinant Tbp2 protein of a *Moraxella catarrhalis* strain M35, 3 or LES1 which comprises:

growing the transformed host of claim 4 to express Tbp2 protein as inclusion bodies,

purifying the inclusion bodies free from cellular material and soluble proteins,

solubilizing Tbp2 protein from the purified inclusion bodies, and

purifying the Tbp2 protein free from other solubilized materials.

6. A recombinant Tbp2 protein of *Moraxella catarrhalis* strain M35, 3 or LES1 producible by the transformed host of claim 4, having a deduced amino acid sequence selected from the group consisting of those shown in Figure 2, 4 or 6 (SEQ ID NO: 2, 4 or 6).

7. An immunogenic composition, comprising at least one active component selected from the group consisting of:

(A) a purified and isolated nucleic acid molecule as claimed in claim 1; or

(B) a recombinant Tbp2 protein as claimed in claim 6;

and a pharmaceutically acceptable carrier therefor, said at least one active component producing an immune response when administered to a host.

8. A method for generating an immune response in a host, comprising administering to the host an immunoeffective amount of the immunogenic composition of claim 7.

9. A method of determining the presence, in a sample, of nucleic acid encoding a transferrin receptor protein of a strain of *Moraxella*, comprising the steps of:

(a) contacting the sample with the nucleic acid molecule of claim 1 to produce duplexes comprising the nucleic acid molecule and any said nucleic acid molecule encoding the transferrin receptor protein of a strain of *Moraxella* present in the sample and specifically hybridizable therewith; and

(b) determining production of the duplexes.

10. A diagnostic kit for determining the presence, in a sample, of nucleic acid encoding a transferrin receptor protein of a strain of *Moraxella*, comprising:

(a) the nucleic acid molecule of claim 1;

(b) means for contacting the nucleic acid molecule with the sample to produce duplexes comprising the nucleic acid molecule and any said nucleic acid present in the sample and hybridizable with the nucleic acid molecule; and

(c) means for determining production of the duplexes.

11. A nucleic acid molecule of claim 1 for use as a medicine.

12. A recombinant transferrin receptor protein of claim 6 for use as a medicine.

13. The use of a nucleic acid molecule of claim 1 in the manufacture of a medicament for protection against infection by a strain of *Moraxella*.

14. The use of a recombinant transferrin receptor protein of claim 6 in the manufacture of a medicament for protection against infection by a strain of *Moraxella*.